Notice of Allowability	Application No. 09/938,013	Applicant(s) NGUYEN ET AL.	
	Examiner Jeanine A Goldberg	Art Unit 1634	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address*--

claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included ewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS TICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative ne Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

☒ This communication is responsive to *11/30/04*.

☒ The allowed claim(s) is/are *4 and 5*.

☐ The drawings filed on _____ are accepted by the Examiner.

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

pplicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements oted below. Failure to timely comply will result in ABANDONMENT of this application.
HIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.

(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.

(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

achment(s)

☐ Notice of References Cited (PTO-892)
☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Jeanine Goldberg

JEANINE A. GOLDBERG
PATENT EXAMINER

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. This examiner's amendment was made as provided by the response in the amendment filed November 30, 2004. The amendments to the specification submitted by applicant were not replacement paragraphs, therefore the following examiner's amendment is required.

3. The application has been amended as follows:

A) The replacement paragraph provided in the response filed November 30, 2004 did not completely replace a paragraph. The following paragraph is to replace the paragraph on page 5-6, beginning at line 16 of page 5. Please replace with

- The synthesis of the cDNA was performed by reverse transcription (RT), described by Sambrook *et al.* [1] The first copies of cDNA were synthesized using two synthesized oligonucleotides SEQ ID NO:1 and 2 (Genosys biotechnologies, Europe. Ltd., France) with the following sequences: 5'CACATTGCATTTG3' (SEQ ID NO:1) and 5'CTGTCTGTCTCA3' (SEQ ID NO:2). These oligonucleotides SEQ ID NO:1 and 2 were selected by taking the complementary sequence to allow RT. The oligonucleotide SEQ ID NO: 1 was based on the SMN sequence described by Lefebvre et al. [16] between base pairs 1097 and 1 109. The oligonucleotide SEQ ID NO:2 was based on

the sequence of the HUMEFIAB gene, encoding for the human elongation factor I-alpha (EFIA), described by Ann *et al.* [20] between base pairs 881 and 892. This HUMEF1AB gene was used as internal standard for the control of the RT-PCR reactions. The M-MLV Reverse Transcriptase enzyme (Gibco BRL®, Life Technologies Sarl, BP 96, 95613 Cergy Pontoise, France) was used for the reverse transcription reaction. This reaction was effected as follows: - -

B) On page 6 of the specification, please replace lines 14-24 with

- - Four synthesized oligonucleotides SEQ ID NO: 3, 4, 5, 6 (Genosys) were used. They have the following sequences: 5'CCAGGTCTAAAATTCAATGG3' (SEQ ID NO: 3) for the forward primer of SMN, 5'CTGTCTGATCGTTTCTTTAG3' (SEQ ID NO: 4) for the reverse primer of SMN, 5'TGTATTGGATTGCCACACG3' (SEQ ID NO: 5) for the forward primer of HUMEF1AB and 5'CTTCAGCTCAGCAAACTTG3' (SEQ ID NO: 6) for the reverse primer of HUMEF1AB. The oligonucleotides of SEQ ID NO: 3 and SEQ ID NO: 5 (forward primers) were based on the SMN and HUMEF1AB sequences between base pairs 661-680 and 672-690 respectively. The oligonucleotides SEQ ID NO: 4 and SQ ID NO: 6 (reverse primers) were based on the SMN and HUMEF1AB sequences between base pairs 957-976 and 705-723 respectively, in this case however, taking the complementary sequence to allow PCR. Amplification was - -

C) On page 8 of the specification, please replace lines 6-16 with

- - The RT products were first amplified by the PCR technique performed in the same conditions as described previously using the synthesized oligonucleotides SEQ ID NO: 5 and 6 for HUMEF1AB gene and the synthesized oligonucleotides SEQ ID NO: 4, 7, 8, 9 for SMN gene. They have the following sequences: 5'GTTTCAGACAAAATCAAAAAG3' (SEQ ID NO: 7)(forward primer), 5'TCCTTAATTTAAGGAATGTGA3' (SEQ ID NO: 8)(reverse primer), 5'GAAATGCTGGCATAGAGCAG3' (SEQ ID NO: 9)(forward primer). The oligonucleotides SEQ ID NO: 7 and SEQ ID NO: 9 (forward primers) were based on exons 7 and 8 of the SMN sequences between base pairs 869-889 and 922-941 respectively. The oligonucleotide SEQ ID NO: 8 (reverse primer) was based on exon 7 of the SMN sequence between base pairs 901 and 921, in this case, however, taking the complementary sequence to allow PCR. The PCR products - -

D) On page 9, please replace line 11 with - - oligonucleotides (SEQ ID NO: 4, 7, 8, 9 for the probes 1 and 2 and SEQ ID NO: 5 and 6 for the probe 3) and the - -

4. The following is an examiner's statement of reasons for allowance.

The claims have been significantly amended to clearly set forth applicant's invention to a quantitative method for diagnosing SMA by quantitatively detecting exon 7 and 8 of the SMN gene.

The closest prior art, Jung et al., teaches a method for RNA isolation using RT-PCR, however Jung does not specifically teach using a nucleic acid consisting of SEQ ID NO: 1 and SEQ ID NO: 2. Jung teaches amplifying the cDNA, however does not specifically teach amplification with a nucleic acid consisting of SEQ ID NO: 3 and 4 and 5 and 6 for HUMEF1AB. Jung further teaches a method of performing a southern blot analysis and quantification of the RT-PCR products of normal subjects, SMA patients and carries. However, Jung does not specifically teach using probes to exon 7 and 8 which consist of a PCR product amplified by a nucleic acid consisting of SEQ ID NO: 7 and 8 for exon 7 and nucleic acid consisting of SEQ ID NO: 9 and 4 for exon 8. Finally, Jung does not specifically teach a range for quantification as provided by the instant claims. As seen in Table 1 and 2 of the instant application, the SMA patients' ranges for quantitation of the probes did not overlap and was outside the range of the control patients sampled. Thus, Jung fails to teach or suggest the claimed invention as a whole.

5. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J. Goldberg

Jeanine Goldberg
Patent Examiner
December 6, 2004